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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,995	03/26/2004	David N. Edwards	068660.0126	9005

31625 7590 08/22/2006

BAKER BOTTS L.L.P.
PATENT DEPARTMENT
98 SAN JACINTO BLVD., SUITE 1500
AUSTIN, TX 78701-4039

EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,995	EDWARDS ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. Claims 4 and 5 claim "a plurality of exogenous promoters". This limitation cannot be found in Application 09/680,738, now US 6,970,607, of which the current application is a continuation. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

The disclosure is objected to because of the following informalities:

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claims 4 and 5 claim "a plurality of exogenous promoters," which is a limitation not found in the specification.

Page 11 of the specification recites □- gal. It is unclear to what type of galactoside Applicants are referring.

Appropriate correction is required.

Claim Objections

Claim 10 is objected to because of the following informalities: A comma is required after dexamethasone in line 5. "Agent" needs to be pluralized in line 7. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 5 comprise "a plurality of exogenous promoters operable to induce expression of the first (second) hybrid protein in the host cell over a wider continuous range of amounts". It is unclear what amounts are being determined.

Claim 10 recites the language "steroids complementary to orphan receptors." Steroids bind receptors; they are not complementary to them.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims the use of any growth factor, cytokine, hormone, their cellular receptors, or fragments thereof, to act as an activator. The claims read on a broad genus of growth factors, cytokines, hormones, their cellular receptors and fragments thereof.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims fragments of growth factors, cytokines, hormones and their cellular receptors by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the use of growth factors, cytokines, hormones and their cellular receptors. The specification does not teach what fragments of growth factors, cytokines, hormones and their cellular receptors would have the capacity to activate a promoter, nor does the specification identify what fragments of these activators are required for their function as

such. Furthermore, in the absence of such identifying characteristics, it would be impossible for the skilled artisan to envision what fragments of growth factors, cytokines, hormones and their cellular receptors had the capacity to activate a promoter. Thus the skilled artisan could not envision what fragments of growth factors, cytokines, hormones and their cellular receptors would be capable of inducing the expression of a gene. Therefore, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification only discloses growth factors, cytokines, hormones and their cellular receptors, and not fragments of them.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of fragments of growth factors, cytokines, hormones and their cellular receptors by disclosing structural or functional features of the fragmented growth factors, cytokines, hormones and their cellular receptors so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of species of the claimed genus. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification.

Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claim Rejections - 35 USC § 102

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 6, 7 and 8 are rejected under 35 U.S.C. §102(e) as being anticipated by US 5,925,523.

Applicants teach a method of detecting an interaction between a bait polypeptide and a prey polypeptide comprising a first construct with an exogenously activatable promoter, a DBD and nucleic acid encoding the bait, a second construct with an exogenously activatable promoter, a TAD and nucleic acid encoding the prey and a reporter used to detect the interaction. The promoters are activated to induce expression of the proteins and the detection of the interaction can be continuously

adjusted by altering the amount of one of the proteins. Continuous adjustment can be achieved through activation of the first or second promoter and can be made on a dose responsive basis. Also, an agent can be added to interfere with activation. Applicants further teach that one of activators be a steroid, including estrogen or estradiol. The activator could also be a hydrophobic agent or hormone.

US 5,925,523 (specifically columns 24, 26, 29 and 30 and the figures) teaches a two hybrid system for detecting interations between proteins in prokaryotic or eukaryotic cells. In one example, the first hybrid protein comprises the DNA binding domain of the bacteriophage λcI fused to the dimerization domain of GAL4 and the second hybrid protein comprises the α subunit of RNA polymerase and $GAL11^P$ which can interact with the GAL4 dimerization domain (col. 14-15). The reference also provides for adding a modulator that can be an inhibitor, which therefore interferes with the activation of one of the promoters. Detection of the reporter gene expression provides a means for determining a compound's efficacy of potentiating interaction between the proteins. This can be accomplished by generating dose response curves from reporter gene expression. These hybrids are inducibly expressed by the addition of IPTG (which induces lac operators by binding lac repressor which causes it to no longer bind the operator thus allowing transcription). Increasing the amount of IPTG added, increases the amounts of the two hybrids which results in increased expression of the detectable reporter gene, β-galactosidase, as is shown in Figure 2B. Thus, US 5,925,523 teaches a two hybrid system that is continuously adjustable because it is plurally stepped dose-

responsive, consistent with the definition of "continuously adjustable" taught in the specification on (p. 14, lines 23-25).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 6-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,925,523 in view of WO 97/31113.

Claims 1-3 and 6-13 teach the method as described above, however, one of the activators is a steroid. It can be a hormone, specifically estrogen, or a hydrophobic agent.

Claims 14-21 teach a method of detecting an interaction between a bait polypeptide and a prey polypeptide comprising a first construct with an estrogen-sensitive promoter, a GAL4 BD and nucleic acid encoding the bait, a second construct with a glucocorticoid-sensitive promoter, a GAL4 TAD and nucleic acid encoding the prey and a reporter used to detect the interaction. The promoters are activated to induce expression of the proteins and the detection of the interaction is by activation of a LacZ reporter. Detection of LacZ is by colorimetric analysis. Continuous adjustment of the amount of the proteins can be achieved through activation of the estrogen-sensitive or glucocorticoid-sensitive promoter. Applicants further teach that one of activators is estrogen or glucocorticoid. Continuous adjustment of the amount of the proteins also can be achieved through altering the amount of estrogen or glucocorticoid.

US 5,925,523 (specifically columns 24, 26, 29 and 30 and the figures) teaches the claimed invention as described above. However, US 5,925,523 does not teach one of the activators being a steroid, hormone, specifically estrogen. It also does not teach using an estrogen-sensitive promoter or a glucocorticoid-sensitive promoter.

WO 97/31113 (Figures 1, 3 and examples 1, 3, 4, 6 and 8) teaches a two-hybrid assay with estrogen as an activator. Specifically, it teaches plasmids with a GAL4 BD and GAL4 TAD. For example, one plasmid encoded a GAL4-vSrc kinase- Zeta ITAM fusion protein that is estrogen regulated. Another encoded a GAL4-vSrc kinase- Beta ITAM fusion protein that is estrogen regulated. (Other vectors with estrogen receptor domains are described in example 1.) WO 97/31113 also teaches use of glucocorticoid receptors and ligands substituted for or in addition to estrogen receptors and ligands (p.

17). The promoters are activated with estrogen (or glucocorticoid) and a colorimetric assay is performed to detect interaction. The reporter can be LacZ.

The ordinary skilled artisan, desiring to perform a method of detecting an interaction between a bait polypeptide and a prey polypeptide comprising a first construct with an exogenously activatable promoter, a DBD and nucleic acid encoding the bait, a second construct with an exogenously activatable promoter, a TAD and nucleic acid encoding the prey and a reporter used to detect the interaction, wherein the promoters can be estrogen-sensitive or glucocorticoid-sensitive, are activated to induce expression of the proteins and the detection of the interaction can be continuously adjusted by altering the amount of one of the proteins, wherein continuous adjustment can be achieved through activation of the first or second promoter and can be made on a dose responsive basis, and wherein an agent can be added to interfere with activation would have been motivated to combine the teachings of US 5,925,523 on a two hybrid system for detecting interactions between proteins in prokaryotic or eukaryotic cells and detection of reporter gene expression providing a means for determining a compound's efficacy of potentiating interaction between the proteins, by generating dose response curves from reporter gene expression, with the teachings of WO 97/31113, teaching a two-hybrid assay with estrogen or glucocorticoid as an activator. There would be motivation to combine these references because WO 97/31113 states that since compounds introduced into a cell may be labile and therefore not present for long periods of time, it would be advantageous to have all the components present in the cell at the time the cells are exposed to test compounds, and constructs encoding fusion

proteins containing hormone binding domains allows for this. It would have been obvious to one of ordinary skill in the art to use hormone receptors and ligands because WO 97/31113 indicates that the regulatory properties of a hormone ligand binding domain allow the post-translational regulation of interaction of fusion proteins. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,925,523 in view of WO 97/31113 et al and in further view of Yavuzer et al..

Claims 1-3 and 6-21 teach the method as described above. Claims 4 and 5 add the limitation that a plurality of promoters be used in the methods.

US 5,925,523 and WO 97/31113 teach the limitations as described above. However, they do not teach the use of a plurality of promoters.

Yavuzer et al (Gene, 165: 93-96, 1995, see Abstract, Figure 1, p. 96) teach using multiple promoters in a two-hybrid assay.

The ordinary skilled artisan, desiring to use a plurality of promoters in a method of detecting an interaction between a bait polypeptide and a prey polypeptide, would have been motivated to combine the teachings to use multiple promoters in the described methods, since Yavuzer et al teach that multiple promoters operate under different conditions to express different combinations of protein domains without the need for subcloning. It would have been obvious for the ordinary skilled artisan to use

multiple promoters because Yavuzer et al teach that multiple promoters can aid in performing both *in vivo* and *in vitro* testing. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 3 of U.S. Patent No. 6,790,607.

Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons:

Claims 1, 9 and 10 are directed a method of detecting an interaction between a bait and prey polypeptide, claims 2 and 3 of U.S. Patent No. 6,790,607, are also directed to a method of detecting an interaction between a bait and prey polypeptide. Specifically, claims 2 and 3 of U.S. Patent No. 6,790,607 comprise a method of detecting an interaction between a bait polypeptide and a prey polypeptide comprising a first construct with an exogenously activatable promoter, a DBD and nucleic acid encoding the bait, a second construct with an exogenously activatable promoter, a TAD and nucleic acid encoding the prey and a reporter used to detect the interaction. The promoters are activated to induce expression of the proteins and the detection of the interaction can be continuously adjusted by altering the amount of one of the proteins. Continuous adjustment can be achieved through activation of the first or second

promoter and can be made on a dose responsive basis. The activators are a steroid, steroid mimic or steroid analog. Claim 3 narrows the activator to a cortisol, hydrocortisone, estrogen, estradiol, estrone, progesterone, androgen, ecdysone, retinoid, steroids which bind orphan receptors, mineralcorticoid, and mineralcorticoid analogs.

Claims 1 and 9 in the instant application claim the same method steps, but in slightly different order. The difference is negligible as some of the steps are interchangeable. For example, the method in claim 2 of U.S. Patent No. 6,790,607 teaches the composition of the hybrid proteins before describing the introduction of the nucleic acid constructs encoding the hybrid proteins into the host cell. Claim 1 of the instant application merely switched the order, and describes the introduction of the nucleic acid constructs encoding the hybrid proteins into the host cell before teaching the composition of the hybrid proteins. *Ex parte Rubin*. 128 USPQ 440 (Bd. App. 1959) stated that a prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render *prima facie* obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps. See MPEP § 2144.04. Claim 10 of the instant application lists the same activators as claim 3 in U.S. Patent No. 6,790,607, except that it adds dexamethasone as another potential activator. It would be obvious to add dexamethasone, as it is just another steroid in the list.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER